```
=> d his

     (FILE 'HOME' ENTERED AT 16:16:51 ON 24 SEP 2002)

     FILE 'MEDLINE' ENTERED AT 16:16:58 ON 24 SEP 2002
L1            80 S "HHV6"
L2          1024 S "HHV-6"
L3             5 S "40247"
L4             0 S L3 AND L1
L5             0 S L2 AND L3
                 E GALLO C/AU
                 E GALLO R C/AU
L6           831 S E3
L7             0 S L1 AND L6
L8            27 S L2 AND L6
L9            11 S ANTIBOD? AND L8
L10            0 S ATCC AND L8
L11            0 S L6 AND ATCC
L12            9 S DETECT? AND L8
                 E SALAHUDDIN S Z/AU
L13          102 S E3
L14           68 S L6 AND L13
L15           10 S L14 AND L2
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=> d l15 1-10

L15 ANSWER 1 OF 10 MEDLINE
AN 91374623 MEDLINE
DN 91374623 PubMed ID: 1654455
TI Identification of the human herpesvirus 6 glycoprotein H and putative large tegument protein genes.
AU Josephs S F; Ablashi D V; **Salahuddin S Z**; Jagodzinski L L; Wong-Staal F; **Gallo R C**
CS Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda, Maryland 20892.
SO JOURNAL OF VIROLOGY, (1991 Oct) 65 (10) 5597-604.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
OS GENBANK-M64578; GENBANK-M64579; GENBANK-M64580; GENBANK-M64581; GENBANK-M64582; GENBANK-M64583; GENBANK-S57426; GENBANK-S57427; GENBANK-S57509; GENBANK-S57540
EM 199110
ED Entered STN: 19911108
Last Updated on STN: 19970203
Entered Medline: 19911022

L15 ANSWER 2 OF 10 MEDLINE
AN 91370737 MEDLINE
DN 91370737 PubMed ID: 1654146
TI Human herpesvirus-6 (**HHV-6**) (short review).
AU Ablashi D V; **Salahuddin S Z**; Josephs S F; Balachandran N; Krueger G R; **Gallo R C**
CS National Cancer Institute, NIH, Bethesda, MD 20892.
SO IN VIVO, (1991 May-Jun) 5 (3) 193-9. Ref: 33
Journal code: 8806809. ISSN: 0258-851X.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; AIDS
EM 199110
ED Entered STN: 19911108
Last Updated on STN: 19970203
Entered Medline: 19911023

L15 ANSWER 3 OF 10 MEDLINE
AN 91361545 MEDLINE
DN 91361545 PubMed ID: 1653487
TI Genomic polymorphism, growth properties, and immunologic variations in human herpesvirus-6 isolates.
AU Ablashi D V; Balachandran N; Josephs S F; Hung C L; Krueger G R; Kramarsky B; **Salahuddin S Z**; **Gallo R C**
CS Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, Maryland 20892.
NC AI24224 (NIAID)
BRSG-SO7PR05373-28 (DRS)
SO VIROLOGY, (1991 Oct) 184 (2) 545-52.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals; AIDS
EM 199110
ED Entered STN: 19911027
Last Updated on STN: 19970203
Entered Medline: 19911009

L15 ANSWER 4 OF 10 MEDLINE
AN 90179064 MEDLINE
DN 90179064 PubMed ID: 2560617
TI Persistent active herpes virus infection associated with atypical polyclonal lymphoproliferation (APL) and malignant lymphoma.
AU Krueger G R; Manak M; Bourgeois N; Ablashi D V; **Salahuddin S Z**; Josephs S S; Buchbinder A; **Gallo R C**; Berthold F; Tesch H
CS Department of Pediatrics, University of Cologne, FRG.
SO ANTICANCER RESEARCH, (1989 Nov-Dec) 9 (6) 1457-76.
Journal code: 8102988. ISSN: 0250-7005.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199004
ED Entered STN: 19900601
Last Updated on STN: 19980206
Entered Medline: 19900412

L15 ANSWER 5 OF 10 MEDLINE
AN 89338976 MEDLINE
DN 89338976 PubMed ID: 2759346
TI Utilization of human hematopoietic cell lines for the propagation and characterization of HBLV (human herpesvirus 6).
AU Ablashi D V; Lusso P; Hung C L; **Salahuddin S Z**; Josephs S F; Llana T; Kramarsky B; Biberfeld P; Markham P D; **Gallo R C**
CS Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, MD 20892.
SO DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1989) 70 139-46.
Journal code: 0427140. ISSN: 0301-5149.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198909
ED Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890911

L15 ANSWER 6 OF 10 MEDLINE
AN 89097309 MEDLINE
DN 89097309 PubMed ID: 2463490
TI Productive dual infection of human CD4+ T lymphocytes by HIV-1 and **HHV-6**.
AU Lusso P; Ensoli B; Markham P D; Ablashi D V; **Salahuddin S Z**; Tschachler E; Wong-Staal F; **Gallo R C**
CS Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda, Maryland 20892.
SO NATURE, (1989 Jan 26) 337 (6205) 370-3.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 198902
ED Entered STN: 19900308

Last Updated on STN: 19970203
Entered Medline: 19890221

L15 ANSWER 7 OF 10 MEDLINE
AN 89034576 MEDLINE
DN 89034576 PubMed ID: 3182954
TI Polymerase chain reaction amplification and in situ hybridization for the detection of human B-lymphotropic virus.
AU Buchbinder A; Josephs S F; Ablashi D; **Salahuddin S Z**; Klotman M E; Manak M; Krueger G R; Wong-Staal F; **Gallo R C**
CS Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda, Maryland 20892.
SO JOURNAL OF VIROLOGICAL METHODS, (1988 Sep) 21 (1-4) 191-7.
Journal code: 8005839. ISSN: 0166-0934.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 198812
ED Entered STN: 19900308
Last Updated on STN: 19980206
Entered Medline: 19881221

L15 ANSWER 8 OF 10 MEDLINE
AN 89034574 MEDLINE
DN 89034574 PubMed ID: 3182953
TI Molecular studies of **HHV-6**.
AU Josephs S F; Ablashi D V; **Salahuddin S Z**; Kramarsky B; Franza B R Jr; Pellett P; Buchbinder A; Memon S; Wong-Staal F; **Gallo R C**
CS Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda, Maryland 20892.
SO JOURNAL OF VIROLOGICAL METHODS, (1988 Sep) 21 (1-4) 179-90.
Journal code: 8005839. ISSN: 0166-0934.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198812
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19881221

L15 ANSWER 9 OF 10 MEDLINE
AN 89034569 MEDLINE
DN 89034569 PubMed ID: 2846608
TI Antibody prevalence to HBLV (human herpesvirus-6, **HHV-6**) and suggestive pathogenicity in the general population and in patients with immune deficiency syndromes.
AU Krueger G R; Koch B; Ramon A; Ablashi D V; **Salahuddin S Z**; Josephs S F; Streicher H Z; **Gallo R C**; Habermann U
CS Immunopathology Section, University of Cologne, F.R.G.
SO JOURNAL OF VIROLOGICAL METHODS, (1988 Sep) 21 (1-4) 125-31.
Journal code: 8005839. ISSN: 0166-0934.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 198812
ED Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19881221

L15 ANSWER 10 OF 10 MEDLINE
AN 87315412 MEDLINE
DN 87315412 PubMed ID: 3627265
TI HBLV (or **HHV-6**) in human cell lines.
AU Ablashi D V; **Salahuddin S Z**; Josephs S F; Imam F; Lusso P; **Gallo R C**; Hung C; Lemp J; Markham P D
SO NATURE, (1987 Sep 17-23) 329 (6136) 207.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Letter
LA English
FS Priority Journals
EM 198710
ED Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19871019

=> d l15 1-10 ab

L15 ANSWER 1 OF 10 MEDLINE
AB Determination of the nucleotide sequences of two molecular clones of human herpesvirus 6 (**HHV-6**) (strain GS) and comparison with those of human cytomegalovirus (HCMV) has allowed the identification of the genes for the glycoprotein H (gH) and the putative large tegument protein of **HHV-6**. Two molecular clones of fragments of **HHV-6**, the BamHI-G fragment (7,981 bp) of the clone termed pZVB43 and a HindIII fragment (8,717 bp) of the clone termed pZVH14, represent approximately 10% of the **HHV-6** genome (16,689). An open reading frame within the BamHI-G fragment was designated the gH gene of **HHV-6** because of the extensive sequence similarity of its predicted product (79,549 Da) to the HCMV gH gene product. The predicted product (239,589 Da) of an open reading frame within clone pZVH14 showed homology to the predicted product of the proposed gene of HCMV representing the large tegument protein. Computer analyses indicated a closer relationship of the predicted peptides of these **HHV-6** genes to those of HCMV than to those of the other human herpesviruses Epstein-Barr virus, herpes simplex virus type 1, and varicella-zoster virus. The gH gene was more conserved among the human herpesvirus group, while significant sequence similarity of the tegument gene could be found only with that of HCMV. The data reported here with one conserved gene (gH) and a more divergent gene (tegument) support previous reports that **HHV-6** and HCMV are more closely related to each other than to the other well-characterized human herpesviruses.

L15 ANSWER 2 OF 10 MEDLINE
AB Human Herpesvirus-6 is the etiological agent of Roseola infantum and approximately 12% of heterophile antibody negative infectious mononucleosis. **HHV-6** is T-lymphotropic, and readily infects and lyses CD4+ cells. The prevalence rate of **HHV-6** in the general population is about 80% (as measured by IFA) with an IgG antibody titer of 1:80. A lower prevalence, however, is observed in some countries. **HHV-6** is reactivated in various malignant and non-malignant diseases as well as in Chronic Fatigue Syndrome and transplant patients. Furthermore, elevated antibody titers were also observed in lymphoproliferative disorders, auto-immune diseases and HIV-1 positive AIDS patients. There appears to be some strain variability in **HHV-6** isolates. The GS isolates of **HHV-6** (prototype) was resistant to Acyclovir, Gancyclovir, but its replication was inhibited by Phosphonoacetic acid and Phosphoformic acid. HHV-7 isolated from healthy individuals showed, by

restriction analysis, that 6 out of 11 probes derived from two strains of **HHV-6**, cross-hybridized with DNA fragments, derived from HHV-7.

L15 ANSWER 3 OF 10 MEDLINE

AB Fifteen human herpesvirus-6 (**HHV-6**) isolates from normal donors and patients with AIDS, systemic lupus erythematosis, chronic fatigue syndrome, collagen-vascular disease, leukopenia, bone marrow transplants, Exanthem subitum (roseola), and atypical polyclonal lymphoproliferation were studied for their tropism to fresh human cord blood mononuclear cells, growth in continuous T cell lines, reactivity to monoclonal antibodies, and by restriction enzyme banding patterns. All isolates replicated efficiently in human cord blood mononuclear cells, but mitogen stimulation of the cells prior to infection was required. The ability to infect continuous T-cell lines varied with the isolates. Isolates similar to GS prototype infected HSB2 and Sup T1 cells and did not infect Molt-3 cells, whereas isolates similar to Z-29 infected Molt-3 cells but not HSB2 and Sup T1 cells. Some of the monoclonal antibodies directed against the **HHV-6** (GS) isolate showed reactivity with all isolates tested, but others only reacted with **HHV-6** isolates similar to the GS isolate and not with those similar to Z-29 isolate. Restriction enzyme analysis using EcoRI, BamHI, and HindIII revealed that **HHV-6** isolates from roseola, bone marrow transplant, leukopenia, and an HIV-1-positive AIDS patient from Zaire (Z-29) were closely related but distinct from GS type **HHV-6** isolates. Based on the above findings, we propose that, like herpes simplex virus types 1 and 2, the 15 **HHV-6** isolates analyzed can be divided into group A (GS type) and group B (Z-29 type).

L15 ANSWER 4 OF 10 MEDLINE

AB This study focuses on lymphoproliferative diseases associated with persistent infection by Epstein-Barr virus (EBV) and human herpes virus 6 (**HHV-6**). A suggestive premalignant lymphoproliferative state is distinguished from malignant lymphoma and identified as "atypical polyclonal lymphoproliferation" (APL). Sixteen cases of herpes virus (HHV)-associated APL are compared with 21 cases of HHV-associated malignant lymphomas (ML), with 108 cases of EBV or **HHV-6** related acute infections mononucleosis, with 14 cases of seronegative non-specific lymphoid hyperplasia and with 304 cases of HHV-unrelated ML. Six cases of APL and two ML occurred in AIDS patients, two cases in Sjogren's syndrome, one in a kidney allograft recipient, and the remaining cases had no identified underlying disease. APL was histologically reminiscient of excessive infectious mononucleosis, while other cases of Castleman's disease or even of malignant lymphoma. Seropositive APL and ML contained significantly more virus genome than is found in latent background infection. There was no histologic difference between **HHV-6** or EBV-positive APL or ML, although both viruses infect different lymphocyte populations. From histology alone, seropositive ML cases were not distinguished from seronegative ones, yet persistent active EBV and **HHV-6** appear to predominate in follicular center cell- and immunoblastic lymphoma and in HOdgkin's disease. Although no a direct oncogenic activity of these viruses could be observed in our cases, they may contribute to lymphomagenesis by inducing progressive lymphoproliferation.

L15 ANSWER 5 OF 10 MEDLINE

AB In 1986, we reported the discovery and isolation of a novel human herpesvirus (HBLV) from AIDS and other lymphoproliferative disorders. Because HBLV is distinct from other members of the herpesvirus family and can infect B- and T-lymphocytes and other human cells (megakaryocytes and glioblastoma cells), we suggested human herpesvirus-6 (**HHV-**

6) as the taxonomic designation for this virus. In cultures from patients' peripheral blood, the evidence of HBLV can be recognized from the appearance of short-lived giant cells (2-10%), which are large, refractile, and are often mono- and binucleated. As these cells degenerate, extracellular virus particles are found in the culture medium. HBLV can infect fresh mononuclear cells, established B- and T-lymphoblastoid cell lines, megakaryocytes and glioblastoma cell lines. HBLV infection can be detected by: a. morphological changes; b. indirect immunofluorescence assay, in situ hybridization, southern blot analysis, polymerase chain reaction amplification; and c. electron microscopy. Because of its wide cell tropism, HBLV DNA sequences have been detected in B-cell lymphomas and short term cultured cells from Sjogren's patients. Expression of HBLV RNA was also detected in sarcoidosis. The etiological role of HBLV in human tumors is unclear. While in vitro data may not necessarily apply to in vivo conditions, the infection of various cell lines from tumors and fresh mononuclear cells suggests HBLV involvement in a variety of diseases.

L15 ANSWER 6 OF 10 MEDLINE

AB Although infection by HIV-1 has been implicated as the primary cause of AIDS and related disorders, cofactorial mechanisms may be involved in the pathogenesis of the disease. For example, several viruses commonly detected in AIDS patients and capable of transactivating the long terminal repeat of HIV-1, such as herpesviruses, papovaviruses, adenoviruses and HTLV-I have been suggested as potential cofactors. Another candidate is human herpesvirus-6 (**HHV-6**, originally designated human B-lymphotropic virus), which has not only been identified in most patients with AIDS by virus isolation, DNA amplification techniques and serological analysis, but is also predominantly tropic and cytopathic in vitro for CD4+ T lymphocytes. Here we demonstrate that **HHV-6** and HIV-1 can productively co-infect individual human CD4+ T lymphocytes, resulting in accelerated HIV-1 expression and cellular death. We also present evidence that **HHV-6** transactivates the HIV-1 long terminal repeat (LTR). These observations indicate that **HHV-6** might contribute directly or indirectly to the depletion of CD4+ T cells in AIDS.

L15 ANSWER 7 OF 10 MEDLINE

AB Polymerase chain reaction amplification (PCR) is a recently described technique that allows for the amplification of a given sequence of DNA. It can be used to reliably amplify sequences of up to 3 kb within hours. The amplified sequence can then be recognized by hybridization with a specific probe after transfer onto nitrocellulose or nylon paper. We used PCR to recognize human B-lymphotropic virus (HBLV or **HHV-6**) specific sequences in various tumors as well as in the blood of patients with AIDS. Sixty-three specimens of DNA extracted from peripheral blood of patients with AIDS as well as DNA extracted from various lymphoproliferative disorders were analysed; 52 out of 63 (83%) patients with AIDS were found to have amplification of the **HHV-6** specific sequence; 2 out of the 63 (3%) had equivocal amplification and 9 (14%) were found to be negative. Twenty out of 23 tumors were found to have amplified HBLV-specific sequences. Only one of these tumors was positive by Southern hybridization on restriction enzyme digested genomic DNA. In situ hybridization of clinical specimens using radiolabelled RNA probes or hapten-labelled DNA probes was used to detect the presence of HBLV in tumors. Three tumors of B cell origin were found to be positive for HBLV.

L15 ANSWER 8 OF 10 MEDLINE

AB Methods for the purification of enveloped **HHV-6** virions and the viral DNA are presented. The viral genome is estimated to be 170,000 base pairs in size and does not appear to contain inversions

due to absence of submolar bands by restriction enzyme analyses. The genomes of two independent **HHV-6** isolates, HHV-6GS and HHV-6Z29, showed restriction enzyme site pleomorphism. Large scale purification of enveloped **HHV-6** was achieved by continuous flow centrifugation utilizing sucrose gradients, DNAse 1 treatment and banding on 10-30% Dextran T10 gradients. The viral proteins were visualized on high resolution two dimensional polyacrylamide gels and the proteins recognized by serum antibody from patient GS were detected by HR2D Western blot analysis and radioimmunoprecipitation assay. The major antigenic proteins were 200, 120, 80, 72, 30 and 19 kDa.

L15 ANSWER 9 OF 10 MEDLINE

AB Detailed serologic screening showed an antibody prevalence to HBLV (**HHV-6**) in the general population of 26% if very strict criteria for antibody positivity were applied. Lower and borderline antibody titers yet may be found in up to 63% of the population. Only 17% of these persons have clinical symptoms; in the majority infection remains silent. **HHV-6** infection apparently occurs already quite early in life, and initial symptoms can occur, such as short-term high fever, sore throat, local lymphadenopathy and skin rash. Lesions disappear without specific treatment. The frequency of positive antibody tests at higher titers rises in patients with immune deficiency and with atypical lymphoproliferative diseases to 60 and 75%. The rise in antibody titers is associated in patients with immune deficiency by characteristic shifts of blood lymphocyte populations, essentially by increase in immature T-lymphocytes. Highest titers are found in patients with lymphoproliferative syndromes, yet the percentage of atypical lymphoid cells harboring the viral genome is low (about 2% of seropositive patients). Thus it appears, that HBLV, similar to other herpesviruses such as Epstein-Barr virus, usually causes a silent seroconversion, yet may be associated with variable clinical pathology when persisting in an active state. Its pathogenic effect might be rather a cofactor contributing to immune disturbance than overt oncogenicity.

L15 ANSWER 10 OF 10 MEDLINE